



**Armed Forces College of
Medicine
AFCM**

**Antihistamine drugs
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INTENDED LEARNING OBJECTIVES (ILO)



By the end of this lecture the student will be able to:

1. Classify histamine receptors
2. Classify drugs that antagonize the action of histamine
3. Describe the mechanism of action and pharmacologic effects of antihistamines
4. Identify therapeutic uses of antihistamines
5. Explain the adverse reactions of antihistamines.

Synthesis

- Histamine is synthesized by decarboxylation of the amino acid L-histidine with L-aromatic amino acid decarboxylase enzyme.
- L histidine →→ histamine

Storage

■ It is stored in mast cells (in most tissues e.g...)

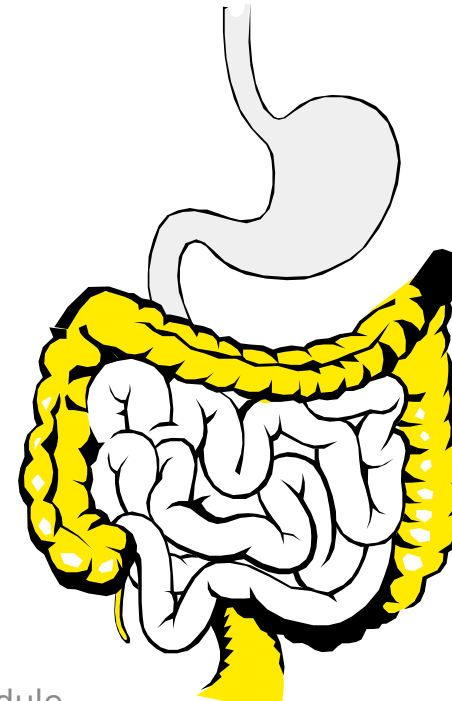
Lung



Skin



GIT



Blood vessels

Release

Immunogenic

**Ag- IgE →
↑ IC. Ca^{2+} →
(Exocytosis)**

Non immunogenic

**(HIC
liberators
)**

**Morphine
Atropine
Curare**

Hydralazine

Histamine receptors

- H1smooth muscles, endothelium, brain leading to contraction in smooth muscles, VD in blood vessels, increased vascular permeability
 - H2 Gastric mucosa, cardiac muscle, brain leading to increased gastric acid secretion and cardiac stimulation
 - Others
-
- All are G protein coupled

Pathogenic role of histamine:

1-Allergy

a. Local allergic response: localized stimulation on blood vessels & nerve endings →

- i. Arteriodilatation → redness.
- ii. Venodilatation → ↑ capillary permeability & edema.
- iii. Sensory nerve stimulation → pain & itching.

b. Anaphylactic shock: generalized stimulation → marked arterial dilatation & hypotension.

c. Bronchial asthma: stimulation on bronchial smooth muscles → bronchospasm.

Pathogenic role of histamine:

2- others

- Vomiting of vestibular origin (e.g. motion sickness) is H1-receptor mediated.
- Peptic ulcer: H2 receptors mediate more than 70% of HCl secretion.

Drugs that antagonize the action of histamine

1. H1 receptor blockers (anti-histamines)
2. H2 receptor blockers for peptic ulcer.
3. Mast cell stabilizers & β 2 agonists: inhibit immunogenic HI release
4. Epinephrine: physiological antagonism.

Antihistamines

First Generation



Promethazine

Chlorpheniramine



Doxylamine



Dimenhydrinate

New generation



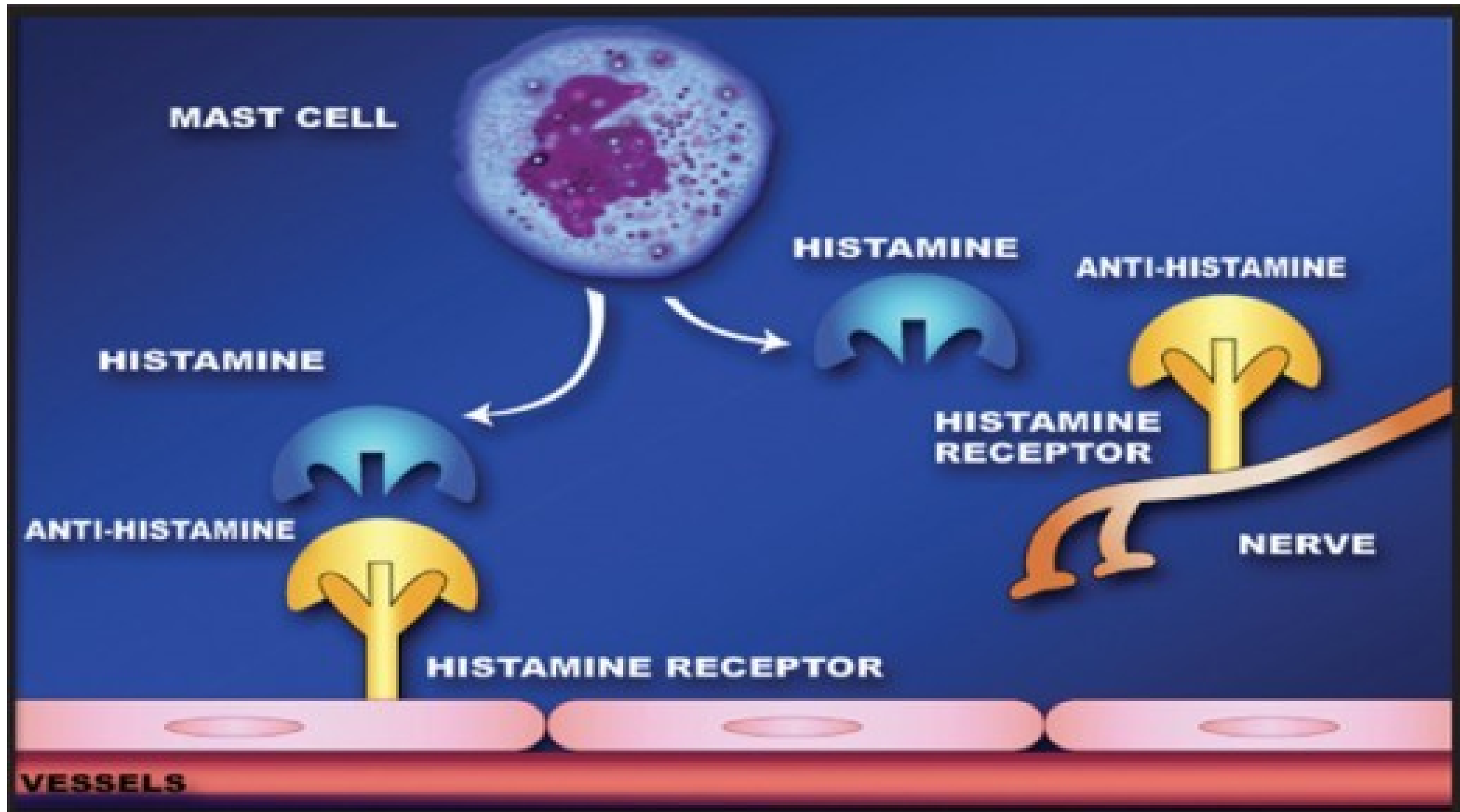
Desloratadine



Fexofenadine



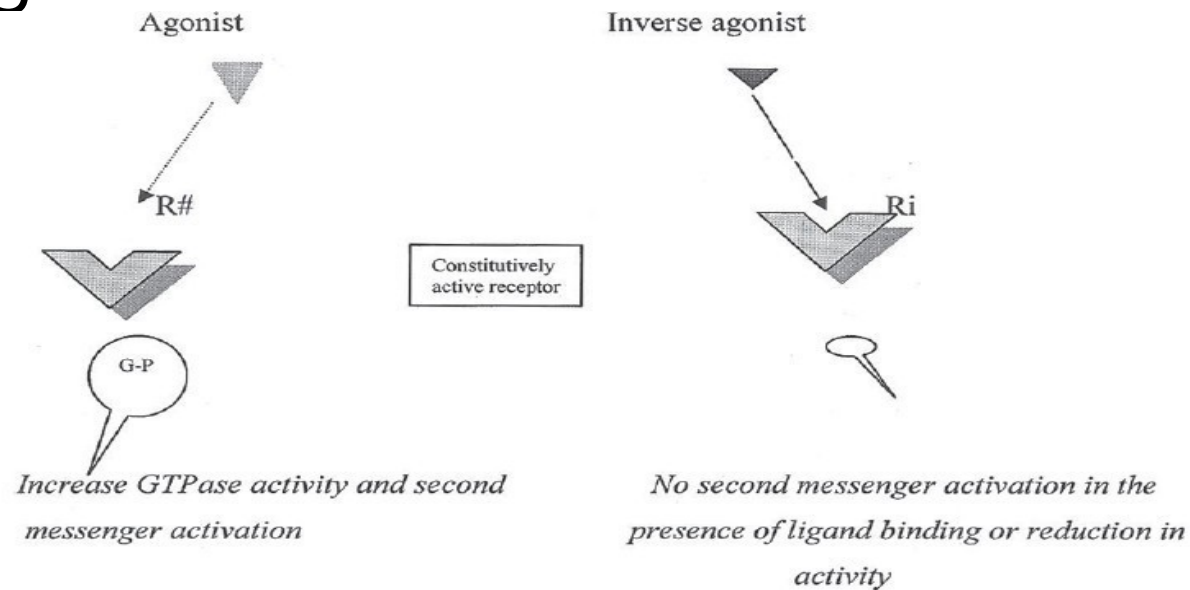
Loratadine



- <https://hubpages.com/health/The-Side-Effects-of-Antihistamines>

First generation mechanism of action

- H1 inverse agonist
- Muscarinic blockers
- Alpha adrenergic blockers



First generation pharmacological action

- **Anti-allergic**
 - Block H1 mediated allergy
- **CNS Depression**
 1. Sedation
 2. Antitussive
- **Muscarinic blockers**
 1. Antiemetic
 2. Antiparkinsonian

First generation therapeutic uses

- **Allergic**

- Rhinitis.
- Urticaria.
- Anaphylactic shock
- Antihistamines are ineffective in asthma → can not antagonize leukotrienes or excessive HI released.

- **CNS Depression**

- OTC hypnotic.
- Dry cough.

- **Muscarinic blockers**

1. Motion sickness
2. Vomiting with pregnancy

First generation side effects

- **Drowsiness, but agitation in children**
- **Atropine-like side effects:**
 - Dry mouth Confusion
 - Urine retention Constipation, Imbalance.
- **Alpha blocking effect:**
 - Postural hypotension

First generation drug interactions

- First G Antihistaminic may decrease effect of cholinesterase inhibitors in Alzheimer disease
- Potentiate effects of sedatives such as alcohol
- Impair driving or operating heavy machinery
- Caution in patients with angle-closure glaucoma, prostatic hypertrophy
- In Elderly patients: It is high-risk medication
 - it may increase risk of falls
 - anticholinergic effects; benign prostatic hyperplasia

New generations Antihistamines

- 1- Less lipophilic → less sedation.**
- 2- Delayed elimination → single daily dosing.**
- 3- Less autonomic side effect**

 **Use → Allergic conditions.**

Still have varying degrees of autonomic effects. High doses can cross BBB → sedation.





A patient is going on a deep sea fishing trip and is worried about motion sickness.

Which of the following would be the most appropriate?

- a. Dimenhydrinate 1 hour prior to departure**
- b. Desloratidine 1 hour prior to departure**
- c. Meclizine at onset of symptoms**
- d. Fexofenadine 1 hour prior to departure**

Lecture Quiz



Your neighbor said she used an H1 antihistamine that was available over the counter, and it caused her marked drowsiness and dry mouth and she slept quite longer than usual. Which is the most possible drug that she used?

- a. Loratidine**
- b. Levocetirizine**
- c. Diphenhydramine**
- d. Fexofenadine**
- e. Desloratidine**

